A Case Report of Small and Medium Vessel Vasculitis As A Spectrum Of Expanded Dengue Syndrome In Central India

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Abstract:

Expanded Dengue Syndrome (EDS) was coined in the WHO guidelines, 2011 to describe the various emerging atypical manifestations of dengue. We report a case of a 22 years old boy, presented in medicine casualty, with high grade fever associated with chills for 7 days along with myalgia, headache and vomiting. He also had multiple painful rashes over bilateral lower limb in form of pinpoint to large discrete macules with few haemorrhagic bullae which progressed in the severity and also developed dry gangrenous changes in index finger of Right upper limb and left great toe. Blood and urine cultures were sterile, and serological markers for malaria and scrub typhus were negative, while dengue serology (ELISA-IgM) was positive. Skin biopsy confirmed Cutaneous small vessel vasculitis (CSVV). Although many cases of EDS with different organ involvement have been reported but extensive vasculitis in form of purpura and gangrene is a rare phenomenon.

Keywords: Dengue, Vasculitis, Expanded Dengue Syndrome

Introduction:

Dengue infection is believed to be caused by dengue virus (DENV), a mosquito borne single positive stranded RNA virus (family: Flaviviridae, genus Flavivirus). There are four related but antigenically distinct serotypes of dengue virus designated as DENV-1, DENV-2, DENV-3, and DENV-4.[1] Dengue virus is transmitted to humans via a mosquito vector, primarily of the genus Aedes (Aedes aegypti & Aedes albopictus).[2] The first infection by one serotype produces lifelong, serotype specific immunity but not lasting protection against infection by

another serotype. The disease is widespread throughout the tropics, with local variations in risk, and is influenced by rainfall, temperature, and unplanned rapid urbanization. The spectrum of disease varies from mild self-limiting illness to dengue fever (DF) to more severe and fulminating forms, i.e., dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).[3,4]

WHO has proposed new dengue classification in 2009. According to this new definition, dengue is classified into two types based on its severity: non-severe dengue (dengue with and without warning signs) and severe dengue.[5] Following the recognition of emerging atypical manifestations of dengue, WHO coined the term "expanded dengue syndrome (EDS)," which includes various clinical features pertaining to different organ systems.[6] The Immuno-pathological mechanisms during dengue infection primarily target endothelium, resulting in vascular permeability and coagulation disorders that result in a spectrum of systemic involvements.[7] This spectrum of Expanded Dengue syndrome involves neurological, Gastro-hepatic, Renal, Cardiac, Respiratory, musculo-skeletal and Lympho-reticular involvement.

The blood vessel is a major target for end-organ damage in dengue, leading to capillary leak. There is a reporting of the rare presentation of Dengue fever with various end-organ damages as EDS such as myocarditis, possibly thrombotic microangiopathy, Cutaneous Small Vessel Vasculitis (CSVV) as purpura, and medium-vessel vasculitis with impending peripheral gangrene.[8] There have also been a few reported cases of dengue with thrombotic microangiopathy, one describing the kidney injury and another resulting in disseminated intravascular coagulation (DIC) and peripheral gangrene. [9,10]

Case Report:

A 22 years old boy, resident of Bhilai, Durg (CG), presented to the emergency casualty with a history of continuous, high-grade fever associated with chills for 7 days along with myalgia, headache and vomiting. Following 5 days of fever he developed multiple painful rashes over bilateral lower limb in form of pinpoint to large discrete macules, below knee. The rashes were reddish at onset, later blackened and also developed few haemorrhagic bullae. Later he developed dry gangrenous changes in index finger of Right upper limb and left great toe after

4 days of developing rashes (day 9 of illness). Patient had history of addiction of tobacco chewing for 4 years with no other co-morbidities.

On Examination patient was pale, afebrile, conscious, oriented, but irritable. Vitals were stable: Heart rate 130 bpm, regular with satisfactory pulse volume. Blood pressure 100/50 mmHg, and pulse pressure of 50 mmHg. He was comfortable with respiratory rate- 16 per minute with oxygen saturation of 95% on room air. Chest examination demonstrated bilateral vesicular breathing with equal air entry on both sides. S1 and S2 were normal, and gallop/murmur not heard. Abdomen was non tender, soft with no organomegaly. All peripheral arterial pulsations were felt. Jugular venous pressure was not elevated. He had Painful palpable purpura (Figure 1) observed in bilateral lower limb below knee, which started darkening & were tender to touch, and also developed dry gangrenous changes in index finger of right upper limb and left great toe from day 4 (day 9 of illness). (Figure 2 & 3)

Electrocardiography showed sinus tachycardia. Chest X-ray was normal. Complete Blood Count on day of presentation showed severe thrombocytopenia (platelet count, 30,000/mm^3), Hemoglobin- 10.8 g/dl, leukocyte count (7800/mm^3) with a peripheral smear showing normochromic normocytic picture. Erythrocyte-sedimentation-rate was 17 mm/h, and C-reactive protein was 24 mg/L. Kidney and Liver function tests were in normal range. NT pro-BNP levels and trans thoracic echocardiogram were also normal. Blood and urine cultures turned out to be sterile, and other infectious markers (malaria, scrub typhus) were negative, except for dengue serology (ELISA-IgM). Serology for hepatitis B, hepatitis C, and human immunodeficiency virus was negative. On day 4 of presentation hemoglobin levels fell to 6.79 g/dl associated with fall in hematocrit levels, but not associated with and overt signs of bleeding suggestive of occult bleeding tendency. Arterial and venous doppler ultrasonography of both lower limbs demonstrated normal flow. A punch skin biopsy was obtained from the area of purpuric rashes, which revealed focal perivascular inflammatory cell infiltrate with nuclear fragmentation in superficial dermis without any granulomas, suggestive of Cutaneous small vessel vasculitis (CSVV).

The final diagnosis of "Expanded Dengue Syndrome with Cutaneous Small Vessel Vasculitis (as purpura) and medium vessel vasculitis (as impending gangrene) with severe thrombocytopenia was made.

He was given titrated intravenous crystalloids, oral tablet prednisolone started at 0.75mg/kg/day and tapered down every 5 days. Tablet Cilastazol was started after the improvement of thrombocytopenia. Initially patient required 8 units of Random donor Platelet (RDP) transfusion considering the evidence of severe thrombocytopenia and occult bleeding. Over the course of hospital stay, he improved symptomatically, platelet counts improved, and features of purpura and impending gangrene improved. On follow-up visit after 7 days, his impending gangrene was not progressing and sloughing had started, and he was followed up in the department of surgery. On a telephonic follow-up after 2 months, he is doing well and leading a normal life.

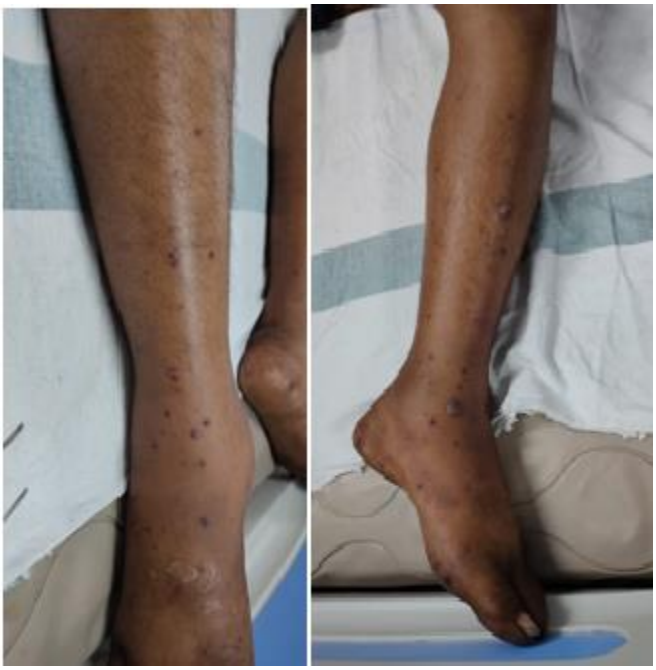

Figure 1: Painful palpable purpura in both lower limb

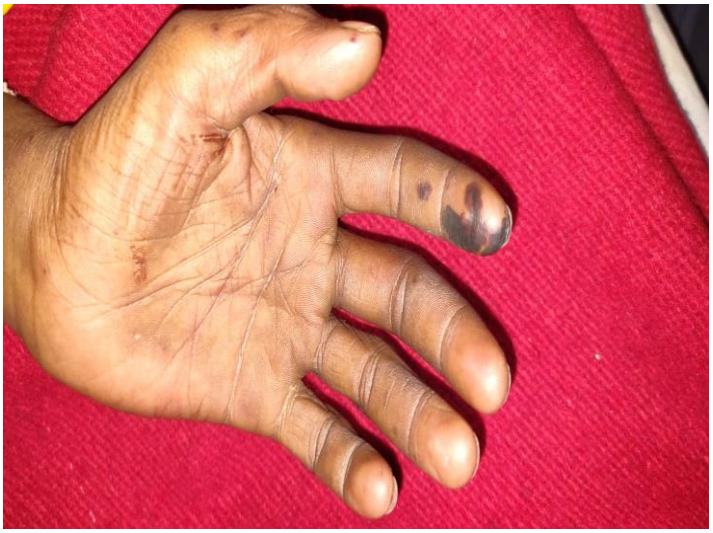

Figure 2: Dry gangrenous changes in index finger of right upper limb

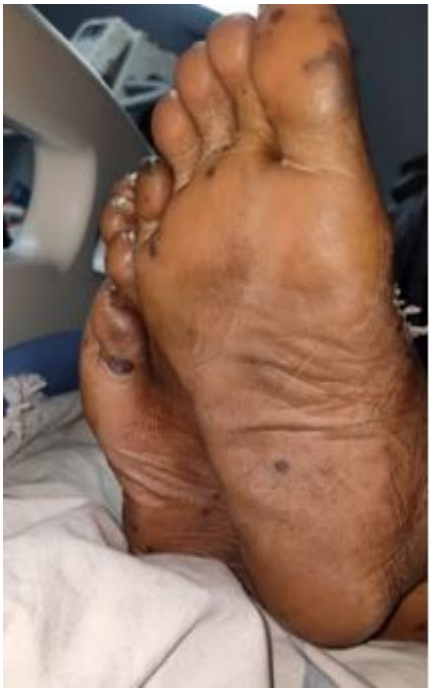

Figure 3: Dry gangrenous changes in left great toe

Discussion:

CSVV is mostly idiopathic and presents as palpable purpura.[11] Few virus infections such as Herpes and Influenza A have been identified as etiological factors of CSVV. [12,13] Only a few cases of cutaneous vasculitis associated with dengue infection have been reported previously.[14,15] Hence, dengue inciting gangrene and purpura without DIC deserves a recognition and may be added to the spectrum of EDS. The management of CSVV is mainly to treat the underlying triggering factor, as it resolves spontaneously in most cases. However, there are evidence of widespread endothelial involvement, which may even trigger Central nervous system vasculitis.

Conclusion:

To conclude, the available evidence supports the assumption of dengue fever resulting in widespread endothelial activation, leading to small and medium vessel vasculitis manifesting as purpura and impending distal dry gangrene of limbs respectively. It also helps treating physicians to suspect for possible atypical complications while managing dengue patients especially in the endemic areas like Central India.

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